REMARKS

Claims 1-5, 7-14, 16-23, 25-32 and 34-42 remain pending in the application. Applicant respectfully requests reconsideration of the claims in view of the following remarks and the Rule 131 Declaration submitted herewith.

The Examiner Interview

Applicants thank Examiner Choi and Examiner Sabiha Naim Qazi for the courtesies extended to Applicants and their representatives during the Examiner interview on June 10, 2005. Applicants believe that the interview was helpful in advancing prosecution of the application. Applicants' summary of the interview, required by 37 C.F.R. § 1.333, is set forth below.

The focus of the interview was the Rule 131 declaration that Applicants submit to antedate the WO 01/10420 publication cited in the Office Action. The examiner indicated that Applicants should submit a declaration that makes clear that the inventive activity took place in the U.S. (or a WTO country), that explains that the components of the tested composition fall within the scope of the claims, and that explains how the test results show that the composition achieves a plasma profile that falls within the scope of the claims. The examiner also indicated that Applicants should submit documentation to support the declaration, such as a document showing the components of the tested composition and data (such as the graph submitted with the previous Rule 131 Declaration) showing that the plasma concentration profile achieved by the tested composition falls within the claims.

During the interview other issues were raised, including the scope of the composition claims and the possible prior art effect of WO 99/30694. It was agreed that the Examiner would give these issues further consideration and raise them in a further, non-final Office Action, if necessary.

Applicants are submitting herewith a Rule 131 Declaration that is believed to address the concerns set forth in the Office Action and discussed during the interview, as explained in more detail below.

The Office Action

The Office Action issued December 15, 2004 makes a § 102 rejection of certain claims over WO 01/10420 (Vickers) and makes a § 103 rejection of other claims over WO 01/10420 and U.S. Patent No. 5,656,286 (Miranda). Because both rejections rely on Vickers as the sole or primary reference, Applicants can overcome this rejection by removing Vickers as prior art against the application.

Vickers was published February 15, 2001, less than one year before the December 21, 2001 filing date of the instant application. Applicants therefore can remove Vickers as prior art by showing that Applicants reduced the invention to practice before Vickers. See 37 CFR § 1.131. The accompanying Rule 131 Declaration effectively antedates Vickers, as shown below.

MPEP 715.02 sets forth several basic principles to keep in mind when evaluating a Rule 131 Declaration. First, the Declaration should establish possession of an embodiment falling within the scope of the claims, such as a species of a claimed genus. Second, the Declaration is sufficient if it establishes possession of as much of the invention as is disclosed in the cited reference. Thus, a Declaration is not insufficient merely because it does not show the identical subject of the claims, as long as it shows a completion of the invention commensurate with the extent of the invention as shown in the cited reference. The Declaration need not be fully commensurate with the claims at issue, because Applicant's possession of what is shown carries with it possession of variations and adaptations which would have been obvious, at the same time, to one of ordinary skill in the art. Of course, the Declaration must establish possession of the invention (i.e., the basic inventive concept).

The Declaration submitted herewith satisfies these requirements and shows that Applicants reduced the invention to practice prior to the publication date of Vickers. The following discussion explains how the Declaration establishes that Applicants reduced the invention to practice (in the U.S.) prior to Vickers, and how the Declaration establishes possession of embodiments within the scope of the claims and possession of at least as much of the invention as is disclosed by Vickers.

I. Independent Claims

A. Claim 1

Claim 1 recites:

> A composition for topical application comprising methylphenidate and a pharmaceutically acceptable adhesive in a flexible, finite system, wherein said composition delivers methylphenidate in an amount and rate sufficient to increase the methylphenidate plasma concentration of a subject being treated over a period of about 6-16 hours, followed by a steady decrease in the plasma concentration of methylphenidate.

The Declaration and Exhibit 2 demonstrate possession of a composition falling within the scope of claim 1 prior to February 15, 2001. Specifically, the Declaration shows that a composition for topical application was made comprising methylphenidate, BIO-PSA 7-4102, and Gelva 3087. Decl. ¶ 4; Ex. 2. BIO-PSA 7-4102 and Gelva 3087 are both adhesives. Id. The composition was prepared as a transdermal patch, i.e., a flexible, finite system. Decl. ¶ 4. Thus, Applicants were in possession of "[a] composition for topical application comprising methylphenidate and a pharmaceutically acceptable adhesive in a flexible, finite system."

The Declaration describes the pharmacokinetics of the composition and Exhibit 3 shows the methylphenidate plasma profiles obtained using the methylphenidate composition tested. Decl. ¶ 6-9. The composition was found to deliver methylphenidate in an amount and rate sufficient to increase the plasma blood concentration of methylphenidate for about 8 hours followed by a steady decrease in the plasma concentration of methylphenidate. Decl. ¶ 7; Ex. 3. This falls within the scope of the claim 1, because 8 hours is within the 6-16 hours range recited. Thus, the Declaration and Exhibits 2 and 3 demonstrate possession of a composition with every feature recited in claim 1.

B. Claim 11

Claim 11 is similar to claim 1 but recites the additional phrase "wherein said composition comprises about 10 to 30 wt% methylphenidate, about 30 to 50 wt% acrylic adhesive, and about 30 to 50 wt% silicone adhesive."

The Declaration and Exhibit 2 demonstrate possession of a composition satisfying the additional recitations of claim 11 because "the composition of the tested transdermal systems comprised 20 wt% methylphenidate, 40 wt% BIO-PSA 7-4102, and 40 wt% Gelva 3087." Decl. ¶ 4; Ex. 2. BIO-PSA 7-4102 is a silicone adhesive, and Gelva 3087 is an acrylic adhesive. Thus, the composition comprised 20 wt% methylphenidate, 40 wt% silicone adhesive, and 40 wt% acrylic adhesive. These quantities fall into the recited range of "10 to 30 wt% methylphenidate, about 30 to 50 wt% acrylic adhesive, and about 30 to 50 wt% silicone adhesive." Accordingly, the Declaration and Exhibits 2 and 3 demonstrate possession of a composition with every feature recited in claim 11.

C. Claims 20 & 29

Claims 20 and 29 are method claims corresponding to claims 1 and 11, directed to a method of treating attention deficit disorder and attention deficit hyperactivity disorder comprising administering a composition as claimed in claims 1 and 11, respectively. As shown above, the Declaration and Exhibits 2 and 3 demonstrate possession of a composition falling within the scope of claims 1 and 11. The Declaration and Exhibit 1 show that the experimental work was performed to support an NDA which "seeks approval to market a transdermal drug delivery system for delivering methylphenidate for the treatment of attention-deficit hyperactivity disorder (ADHD)." Decl. ¶ 2; Ex. 1. In other words, the experimental work was done to obtain regulatory approval for a method of treating ADHD. Thus, the Declaration shows possession of the methods of claims 20 and 29.

II. Dependent Claims

The discussion below shows that the Declaration and Exhibits 1-3 demonstrate possession of an embodiment falling within the scope of the dependent claims, at least to the extent disclosed by Vickers. See MPEP 715.02.

A. Claims 2, 3, 12, 13, 21, 30, 31, and 38

Claims 2, 3, 12, 13, 21, 30, 31 and 38 recite specific embodiments of the methylphenidate plasma concentration profiles. The Declaration and Exhibit 3 shows that,

for the tested composition, the methylphenidate "plasma concentration steadily increased to a maximum of about 8 ng/mL at around 8 hours" and then "steadily decreased to return to the about the starting concentration of 2 ng/mL at 28 hours." Declaration ¶ 7. The 8 hours of increased plasma concentration is within both the 6-12 hour range recited in claims 3, 13, 31 and 38 and the 6-16 hour range recited in claims 12, 21 and 30. In addition, the decrease over a period of about 20 hours meets the recitation of "followed by a steady decrease in the plasma concentration of methylphenidate over a period of at least 8 hours" recited in claims 2, 12, and 30. Thus, the Declaration demonstrates possession of an embodiment falling within the scope of the claims 2, 3, 12, 13, 21, 30, and 31.

B. Claims 4, 5, 14, 22, 23, & 32

Claims 4, 5, 14, 22, 23, and 32 recite specific embodiments of the rate of increase in methylphenidate plasma concentration. The Declaration shows that, for the tested composition, "a rate of increase of about 0.75 (ng/mL)/hr" was achieved, and "is representative of the rate of increase demonstrated in Exhibit 3." Decl. ¶ 8. The 0.75 (ng/mL)/hr rate that was achieved falls within the range of "0.06 (ng/mL)/hr to 6.0 (ng/mL)/hr" recited in claims 4, 14, 22, 32, and the range of "0.4 (ng/mL)/hr to 2.5 (ng/mL)/hr" recited in claims 5 and 23. Thus, the Declaration demonstrates possession of an embodiment falling within the scope of the claims 4, 5, 14, 22, 23, and 32.

C. Claims 10, 19, 28 & 37

Claims 10, 19, 28 and 37 recite specific embodiments of the rate of methylphenidate delivery over 24 hours. As explained in the Declaration, Exhibit 3 demonstrates that the tested composition achieved a methylphenidate delivery of "at least 5 mg per 24 hours," as recited in claims 10, 19, 28, and 37. Decl. ¶ 8. Thus, the Declaration demonstrates possession of an embodiment falling within the scope of the claims 10, 19, 28 and 37.

D. Claims 8, 9, 17, 18, 26, 27, 35, 36

Claims 8, 9, 17, 18, 26, 27, 35, 36 recite delivery of "a therapeutically effective amount" of methylphenidate over a period of "about 12 to about 24 hours" or "over a period

of about 12 to about 18 hours." The Declaration and Exhibit 3 shows that the tested composition achieved delivery of a therapeutic amount of methylphenidate over a period of time falling within these ranges.

The therapeutically effective dose depends on the characteristics of the particular patient, such as body weight, age, and condition severity. As taught in the instant specification, a delivery rate of about 0.5 mg/24 hours to about 100 mg/24 hours is needed to achieve a therapeutically effective dose. Specification, pg. 15. The Declaration and Exhibit 3 show that the tested composition achieved delivery of a of methylphenidate over a period of "about 12 to about 24 hours" and a period of "about 12 to about 18 hours," as recited. Decl. ¶ 9. Thus, the Declaration and Exhibit 3 demonstrate possession of an embodiment falling within the scope of claims 8, 9, 17, 18, 26, 27, 35, 36.

Moreover, according to Vickers, 2 ng/mL is a therapeutic plasma level of methylphenidate for a 30 kg child. As discussed above, the Declaration demonstrates possession of a composition that maintains a methylphenidate plasma concentration of at least 2 ng/mL for over 24 hours. Decl. ¶ 8; Ex. 3. Thus, Applicants have demonstrated possession of at least as much of these embodiments as Vickers discloses. In addition, one of ordinary skill in the art could readily adjust the amount of methylphenidate delivered by changing the size of the patch and/or the methylphenidate loading, as taught in the instant specification.

E. Claims 7, 16, 25, 34 & 39-42

Claims 7, 16, 25, and 34 recite compositions and methods where the composition is "substantially free of ritalinic acid at the time of manufacture," and claims 39-42 recite compositions and methods where the composition "comprises no more than amout 5% weight/weight of acid functional monomers." The Declaration and Exhibit 2 show that the composition tested was "free of ritalinic acid at the time of manufacture" and comprised "no more than about 5% weight/weight of acid functional monomers." Declaration ¶ 4. Thus, the Declaration and Exhibit 2 demonstrate possession of an embodiment with claims 7, 16, 25, 34, and 39-42.

In summary, the Declaration and Exhibits demonstrate reduction to practice in the U.S. of the invention recited in each of the pending claims prior to the publication date of Vickers. Applicants therefore believe that Vickers is effectively removed as a prior art reference against the claims, and that the §102 and §103 rejections are obviated.

CONCLUSION

In view of the foregoing, Applicants believe that the application is in condition for allowance, and an early notice to that effect is earnestly solicited. Should there be any questions regarding this submission, or if any issues remain, the Examiner is invited to contact the undersigned by telephone in order to advance prosecution.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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